

Exhibit 1

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Graduate Program in Immunology, University of Texas Southwestern Medical Center, Dallas 75235-9036.

Prolactin receptor (PRLr) expression and distribution in thymus, spleen, bone marrow, lymph nodes, and peripheral blood lymphocytes from young adult Lewis rats are analyzed using single-color flow cytometry and a well-characterized monoclonal antibody directed against the rat liver PRLr. The in vivo effects of regional immunization on PRLr expression are also examined. PRLr is found to be widely distributed among cells of the immune system and demonstrates lymphoid tissue-specific patterns of expression. Footpad immunization caused the rapid, but transient, induction of PRLr expression in the draining lymph node, with only modest effects on PRLr expression in other distant lymphoid tissues. These studies indicate that PRL may be capable of direct interaction with the immune system through differential expression of the PRL cell surface receptor on select lymphoid target cell populations.

PMID: 8319823 [PubMed - indexed for MEDLINE]

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**Note:** Performing your original search, *human growth hormone and signal peptide*, in PubMed will retrieve 42 citations.

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☐ 1: Gene. 1991 Jan 15;97(2):253-8.

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### **Human interleukin 1 beta fused to the human growth hormone signal peptide is N-glycosylated and secreted by Chinese hamster ovary cells.**

**Pecceu F, Dousset P, Shire D, Cavrois E, Marchese E, Ferrara P, Kaghad M, Dumont X, Lupker J.**

Unite Technologie des Cellules Animales Recombinees, Sanofi Elf Bio Recherches, Labège, France.

A hybrid gene consisting of the sequences coding for the signal peptide of human growth hormone and the mature form of interleukin-1 beta (IL-1 beta) was chemically synthesized. This sequence was inserted into a eukaryotic expression vector and introduced into Chinese hamster ovary cells. The resulting stably transformed cell lines produced large amounts of recombinant IL-1 beta, which was secreted into the culture medium mainly as a 22-kDa form. Expression in the presence of tunicamycin, an inhibitor of N-glycosylation, led to the complete disappearance of the 22-kDa form and the appearance of a new form of 17.5 kDa, indicating that the hybrid protein had been both processed and N-glycosylated. However, transformed cells producing mature IL-1 beta without a signal peptide produced the predicted 17.5-kDa nonglycosylated form. These results suggest that fusion to a heterologous leader sequence allowed IL-1 beta to be translocated across the membrane of the endoplasmic reticulum and to be transported and secreted by the exocytotic pathway.

PMID: 1999289 [PubMed - indexed for MEDLINE]

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